

52906, 33408, AND 12189, NOVEL POTASSIUM CHANNEL FAMILY
MEMBERS AND USES THEREOF

Related Applications

5 This application claims priority to U.S. provisional application number 60/209,845 filed on June 6, 2000, ^{now ABANDONED,} the contents of which are incorporated herein by reference.

Background of the Invention

10 Potassium (K^+) channels are ubiquitous proteins which are involved in the setting of the resting membrane potential as well as in the modulation of the electrical activity of cells. In excitable cells, K^+ channels influence action potential waveforms, firing frequency, and neurotransmitter secretion (Rudy, B. (1988) *Neuroscience*, 25, 729-749; Hille, B. (1992) *Ionic Channels of Excitable Membranes*, 2nd Ed.). In non-excitable cells, they are involved in hormone secretion, cell volume regulation and potentially in cell proliferation and differentiation (Lewis *et al.* (1995) *Annu. Rev. Immunol.*, 13, 623-653). Developments in electrophysiology have allowed the identification and the characterization of an astonishing variety of K^+ channels that differ in their biophysical properties, pharmacology, regulation and tissue distribution (Rudy, B. (1988) *Neuroscience*, 25, 729-749; Hille, B. (1992) *Ionic Channels of Excitable Membranes*, 2nd Ed.). More recently, cloning efforts have shed considerable light on the mechanisms that determine this functional diversity. Furthermore, analyses of structure-function relationships have provided an important set of data concerning the molecular basis of the biophysical properties (selectivity, gating, assembly) and the pharmacological properties of cloned K^+ channels.

25 Functional diversity of K^+ channels arises mainly from the existence of a great number of genes coding for pore-forming subunits, as well as for other associated regulatory subunits. Two main structural families of pore-forming subunits have been identified. The first one consists of subunits with a conserved hydrophobic core containing six transmembrane domains (TMDs). These K^+ channel α subunits participate in the formation of outward rectifier voltage-gated (Kv) and Ca^{2+} -dependent K^+ channels.